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Mathematical Models of Neuronal Spike Activities

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1. Introduction. By many authors, statistical treatments of neuronal spike trains were formulated. From these mesurements, various kind of mathematical models of neuronal spike activities have been presented in recent year. The random walk model, which is constructed on the bases of random fluctuation of membrance potential and threshold value, is considered as fundamental model of neuronal spike activities. In this model, first passage time to the absorbing barrier corresponds to the time length of inter-spike interval. Nevertheless, in many neurophysiological experiments the probability density function (pdf) of this first passage time doesn't seem to correspond to sample histogram. There are many dificulties to decide the parameter of random walk model. It should be noticed that threshold values are time dependent and change in accordance with the condition of that neuron.

Unit neuronal spike activities, simultaneously recorded from the ventromedial nucleus (VMH) and lateral area (LH) in the cat hypothalamus, showed the reciprocal relation (Oomura et al., 1963; 1967). That is, an increase in frequency of the VMH spike reduces the frequency of the LH spike and vice versa. In general the number of spikes in unit time intervals is represented by a Poisson distribution at low frequency and a generalized Poisson distribution at high frequency. Corresponding to these facts, the pdf of interspike interval is represented by an exponential distribution and by a gamma distribution of order 2, or of higher orders, respectively.

In nerve systems, rates of pulses or mean interspike intervals play an important rule for the transmission of information. However, rate of pulse can not be increased infinitely. In VMH or LH, it is increased from 2 cps to 40 cps. The periods in which the neuron can not be excited after each period of excitement, are called refractory period. In order to fit the pdf of interspike interval to sample histograms, notion of refractory period should be introduced to the model. In section 2 , we consider the pdf of interspike interval which is modified gamma distribution. This distribution has the mean that is decreasing for higher order. On the bases of this distribution, autocovariance functions of pulse trains are calculated. In section 3 the mathematical models of inhibit effects between VMH and LH are presented. In section 4, some notes are given for our models.

2. Probability distribution function of interspike intervals and autocovariance function of spike trains. Let spike train be stochastic point process $N(t)$ and interspike interval be random variable T. In general, T contains absolute refractory period, relative refractory period and the period in which membrande potential goes to threshold value with fluctuation.

2.1. First, we consider the case in which relative refractory period is not contained in T. pdf of interspike interval $f_T(t)$ is assumed to be modified gamma distribution of order k;

$$f_T(t) = (\mu/k^2)\,(t-\beta)^{k-1}\, e^{-\frac{\mu}{k}(t-\beta)} / \Gamma(k) \quad , \qquad t \geq \beta$$
$$= 0 \quad , \qquad t < \beta \ ,$$

which takes the maximum value at $t=\beta+\alpha(k-1)/k$. This pdf has Laplace tranceform

$$\varphi_T(\theta) = e^{-\theta\beta}(1+\mu\theta/k)^{-k} \ .$$

It follows that

$$E(T) = \beta + \mu/k , \qquad V(T) = \mu^2/k^3 .$$

These parameters show that the pdf corresponding to high order k has short mean interval μ/k. If k=1 then we have delayed exponential distribution with expectation $\mu+\beta/2$.

The Laplace transform of $P(\Delta N(t)=1 \mid \Delta N(0)=1)$ is given by

$$\phi_T(\theta) = \left(e^{\theta\beta} \left(1+\mu\theta/k^2\right)^k - 1 \right)^{-1}, \tag{2.1}$$

where $\Delta N(t) = N(t+\Delta t) - N(t)$. To obtain the inverse transform of $\phi_T(\theta)$, we use the approximation of $e^{\theta\beta}$,

$$e^{\theta\beta} \cong 1 + \theta\beta + \frac{(\theta\beta)^2}{2!} + \cdots + \frac{(\theta\beta)^n}{n!} .$$

Then partial fraction expansion of $\phi_T(\theta)$ is given by

$$\phi_T(\theta) \cong \frac{1}{A} \sum_{i=0}^{n+k-1} \frac{B_i}{\theta + \pi_i} ,$$

where A , B_i , $i=0,1,\cdots,n+k-1$, are constants and π_i , $i=0,1,\cdots,n+k-1$, are the roots of denominator of right hand side of (2.1). Therefore approximate incerse transform of $\phi_T(\theta)$ becomes

$$g_T(t) \cong \frac{1}{A} \sum_{i=0}^{n+k-1} B_i e^{-\pi_i t} .$$

Then autocovariance function

$$w(t-\tau) = P(\Delta N(t)=1, \Delta N(\tau)=1) - P(\Delta N(t)=1)\, P(\Delta N(\tau)=1)$$

is reduced to

$$w(t-\tau) \cong \frac{B_0}{A^2} \sum_{i=1}^{n+k-1} B_i e^{-\pi_i(t-\tau)} , \qquad t > \tau .$$

If n=k=1 then

$$w(t-\tau) \cong \frac{-1}{(\beta+\mu)^2} e^{-\frac{\mu+\beta}{\mu\beta}(t-\tau)} .$$

If n=1 and k=2 then

$$w(t-\tau) \cong \left(\frac{16}{\beta\mu^2\pi_2\pi_1(\pi_2-\pi_1)}\right)^2 \left(\pi_1 e^{-\pi_2(t-\tau)} - (2\pi_1+\pi_2) e^{-\pi_1(t-\tau)}\right),$$

where

$$\pi_i \approx \frac{1}{2\mu\beta}\left(\mu+8\beta+(-1)^i\sqrt{\mu^2+16\beta}\right), \quad \mu \geqq 16\beta, \quad i=1,2.$$

2.2. The case in which refractory period is random variable. In this section we take into account the relative refractory period which is considered to be changing its length according to the condition of membrance potential. Furthermore we expross the joint length of relative and absolute refractory period by the random variable Z. The pdf of Z, $f_Z(z)$, is assumed to be uniform because we don't have any knowledge about Z, that is

$$f_Z(z) = 1/\beta, \qquad 0 \leqq z \leqq \beta,$$
$$= 0, \qquad \text{otherwise.}$$

We put

$$T = X + Z$$

where X is a random variable corresponding to that part of interspike interval which does not contain the refractory period. The pdf of X is assumed to be modified gamma distribution of order k, as 2.1.

$$f(x) = (\alpha/k^2)^k\, x^{k-1}\, e^{-\frac{k^2}{\alpha}x}/\Gamma(k), \qquad x \geqq 0,$$
$$= 0, \qquad x < 0.$$

The stochastic point process N(t) is considered to be successively generated by T. As in 2.1, the Laplace transform of pdf is reduced to

$$\varphi_T(\theta) = \frac{1-e^{-\theta\beta}}{\theta\beta}\,\frac{1}{(1+\alpha\theta/k^2)^k}.$$

Hence Laplace transform of

$$g_T(t) = P(\,\Delta N(t)=1 \mid \Delta N(0)=1\,)$$

is given by

$$\phi_T(\theta) = \frac{1-e^{-\theta\beta}}{\beta\theta(1+\alpha\theta/k^2)^k-(1-e^{-\theta\beta})}.$$

Again using the approximation

$$e^{-\theta\beta} \simeq 1 - \theta\beta + \frac{(\theta\beta)^2}{2},$$

we obtain the inverse transform of $\phi_T(\theta)$ as follows

$$g_T(t) = (16/A\alpha^2)(1-(1+A\beta/2)e^{-At})$$

where we put $k=2$ and $A = 8(\alpha+\beta)/\alpha$.

Hence the autocovariance function is given by

$$w(t-\tau) = (-16/A\alpha^2)(1+A\beta/2)e^{-A(t-\tau)}.$$

In order to fit $w(t-\tau)$ to the sample autocovariance function calculated from pulse trains, it is necessary to decide the order k. Coefficient of variation of T, CV(T), is effectively used for this purpose. CV(T) is given as follows

$$CV(T) = \left(\frac{1}{k} + \frac{\beta^2 k^2}{12\alpha^2}\right)^{\frac{1}{2}}/(1+k\beta/2\alpha) .$$

3. Inhibitory dffects between two spike trains. In this section we consider two neurons which are connected through some synapses. To show the essential forms of the mathematical theory we describe two models. Let $N_1(t)$ and $N_2(t)$ be two stochastic point processes that represent the activities of two neurons. There are two types of inhibitory effects between $N_1(t)$ and $N_2(t)$. One type is such that $N_1(t)$ is inhibited by $N_2(t)$ and $N_2(t)$ is not affected by $N_1(t)$. The other type is such that $N_1(t)$ and $N_2(t)$ are mutually inhibited. Let us call these two types one-way inhibition and two-way inhibition. Let μ and λ be pulse rates of $N_1(t)$ and $N_2(t)$ respectively. It is natural that refractory periods of neurons are not affected by the activities of other neurons. Therefore we discuss the interspike intervals which don't contain the refractory periods and denote such interspike intervals of $N_1(t)$ and $N_2(t)$ by T_1 and T_2 respectively.

Let $f_i(t)$ be pdf of T_i and $g_i(t)$ be pdf of time intervals which are varied from $f_i(t)$ by means of inhibitory effects of other neuron, i=1,2.

3.1. One-way inhibition. The inhinitions to $N_1(t)$ from $N_2(t)$ are formulated in the following way (Fig. 2). Under the conditions that one $N_1(t)$ spike occurs at time point 0 and $N_2(t)$ spikes in $(0,t)$ occur at time points $t_1, t_2, \cdots, t_n$, the conditional pdf that next $N_1(t)$ spike occurs at time point t is assumed to given by

$$k\, f_1(t) \prod_{i=1}^{n} P(t-t_i) ,$$

where $P(t)$ is any integrable function such that $P(t) \geqq 1$, $t \geqq 0$ and k is a constant determined by the pdf condition. So that unconditional pdf, $g_1(t)$, is given by

$$g_1(t) = k\, f_1(t)\, E\Big[\prod_{i=1}^{n} P(t-t_i)\Big] . \tag{3.1}$$

Again k is determined by the condition

$$\int_0^\infty g_1(t)\, dt = 1 .$$

Now we assume that $N_2(t)$ is Poisson process, then (3.1) is reduced to

$$k\, f_1(t)\, e^{\lambda \int_0^t [P(t-x)-1]\, E[\, dN_2(x)\,]} . \tag{3.2}$$

Furthermore, if $f_1(t)$ is exponential type with mean α, and $P(t-x)=1+p$, $p \geqq 0$, then (3.2) becomes

$$g_1(t) = \left(\frac{1}{\alpha} - \lambda p\right) e^{-\left(\frac{1}{\alpha} - \lambda p\right)t}, \tag{3.3}$$

which is again pdf of exponential type.

If λ of $N_2(t)$ is sufficiently large then by the central limit theorem we may assume that

(i) $\Delta N_2(t)$ is independent of $\Delta N_2(s)$ for all $t \neq s$,

(ii) $\Delta N_2(t)$ has normal distribution $N(\lambda t, \lambda \sigma^2 t)$.

From these assumptions, we obtain

$$(3.4) \qquad g_1(t) = k\, f_1(t)\, e^{\lambda \int_0^t \log P(t-x)\, dx + \frac{\sigma^2 \lambda^3}{2} [\log P(t-x)]^2 dx} .$$

Now if we put

$$P(t-x) = e^p , \qquad p \geqq 0 ,$$

then for the $f_1(t)$ of exponential type , (3.4) becomes

$$[\frac{1}{\alpha} - \lambda p\,(1+\frac{p\sigma^2\lambda^2}{2})]\, e^{-[\frac{1}{\alpha} - \lambda p\,(1+\frac{p\sigma^2\lambda^2}{2})]} ,$$

where

$$(1/\alpha) > \lambda p(1+\frac{p\sigma^2\lambda^2}{2}) .$$

In Fig. 3, we represent the reciprocal relation of spike activities, simultaneously recorded from VMH and LH in the cat (Oomura et al., 1964; 1967). Data were obtained from the cat during sleep and alertness. The abscissa and ordinate of Fig. 3 show the pulse number (p.s.) of LH neuron and VMH neuron respectively. The regression line in the Fig. 3 represents the equation obtained from (3.3) which was fitted to the sample points by means of least square method.

3.2. Two-way inhibition. In the case when two pulse trains are mutually inhibited, equation (3.1) is reduced to the system of equation;

$$(3.5) \qquad \begin{cases} k_1 f_1(t)\, E[\prod_{i=1}^{n} P_2(t-t_i)] = g_1(t) \\ k_2 f_2(t)\, E[\prod_{i=1}^{n} P_1(t-t_i)] = g_2(t) \end{cases}$$

where k_1 and k_2 are the constants determined by the conditions

$$\int_0^\infty g_1(t)\, dt = 1 , \qquad \int_0^\infty g_2(t)\, dt = 1 ,$$

and $P_1(t)$ and $P_2(t)$ represent the inhibitory effects from $N_1(t)$ and $N_2(t)$ to $N_2(t)$ and $N_1(t)$ respectively. Multiplying t to the both sides of (3.5) and integrating with respect to t on $(0, \infty)$, we obtain the relations between expectations of $g_1(t)$ and $g_2(t)$;

$$\alpha^{-1} = \mu^{-1} - \beta^{-1} p$$
$$\beta^{-1} = \lambda^{-1} - \alpha^{-1} p$$

where we have put

$$P_1(t) = 1 + p_1 , \qquad P_2(t) = 1 + p_2 .$$

Finally we obtain

(3.6) $$\alpha^{-1} = \frac{\mu^{-1} - p_2 \lambda^{-1}}{1 - p_1 p_2} , \quad \beta^{-1} = \frac{\lambda^{-1} - \mu^{-1} p_1}{1 - p_1 p_2} .$$

It is easily shown that (3.6) is the generalization of regression line of (3.3).

4. Some notes. In this paper we considered the mathematical models which are different from random walk models. Now some notes on the fundamental ideas of our models are described as follows;

(i) We adopted the function of modified gamma type as the pdf of interspike intervals. But in view of transmission of information, we want to derive this pdf from the pdf of pulse numbers. Because rates of pulse contain some amount of information, there are certain correspondence between pdf of interspike interval and pdf of pulse number.

(ii) Refractory period and threshold value are varied according to the proper conditions of that neurons. It is also natural that they are dependent on time. Therefore the probability that apulse occurs in a small time interval is not stationary. Indeed, many parameters contained in the model are not constant in such sense. The random variables are very useful to interpret these parameters. Random variable Z introduced in 2.2 was considered to contain all such parameters.

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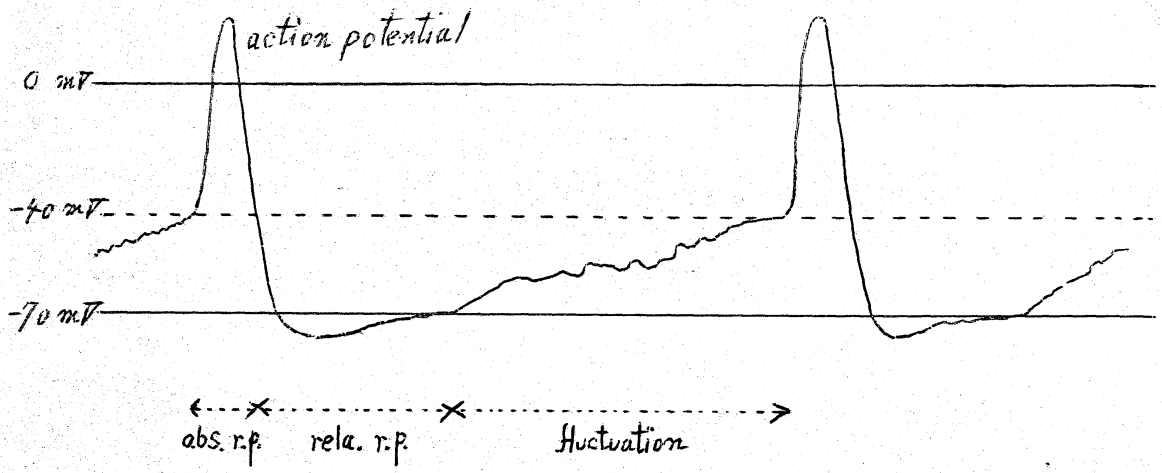

Fig. 1. Fluctuation of Membrance Potential.

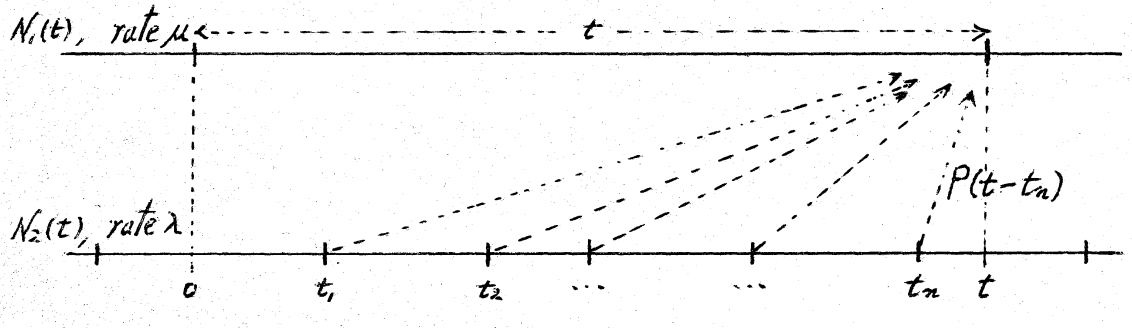

Fig. 2. Inhibitory effects between two spike trains.

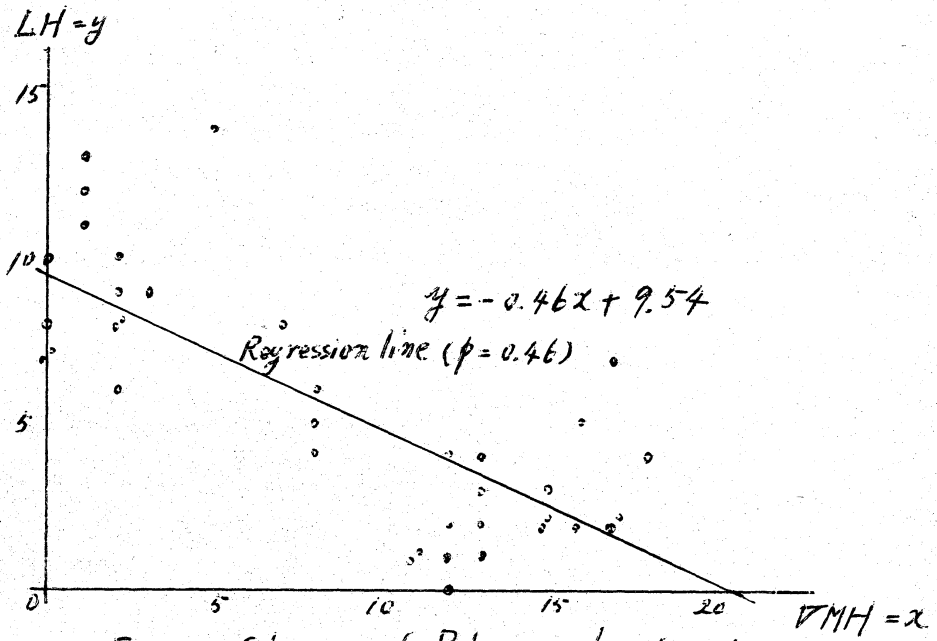

Fig. 3. Changes of Pulse number (p.s.) from sleep to alertness.